

Application No. 10/609,346  
Response Dated November 21, 2006  
Reply to Office Action of August 24, 2006

### **REMARKS/ARGUMENTS**

#### **1. Remarks on the Amendment**

The Specification has been amended to correct typographic and clerical errors.

Claims 21-23, 27-33, 40 and 41 have been cancelled without prejudice.

New Claims 51-67 have been added to more specifically define Applicant's claimed invention.

Antecedent basis of the amendment of independent Claim 51 can be found on page 37, lines 20-31, and page 39, lines 5-11 and of the Specification and claims as filed.

Applicants submit that no new matter has been introduced by the amendment.

#### **2. Response to the Rejection of Claims 21-23, 27-33, 40-41 under 35 U.S.C. §112, first paragraph (Items 2a and 2b of the Office Action)**

Claims 21-23, 27-33, and 40-41 stand rejected under 35 USC §112, first paragraph, as failing to comply with the written description requirement and the enablement requirement. These rejections are respectfully traversed by the amendment.

Claims 21-23, 27-33, and 40-41 have been canceled. However, the rejections have been fully addressed in the new Claims 51-67. Applicants submit that new Claims 51-67 meet the written description and the enablement requirement of 35 USC §112, first paragraph.

Accordingly, Applicants respectfully request withdrawal of the rejection of based upon 35 U.S.C. §112, first paragraph.

Application No. 10/609,346  
Response Dated November 21, 2006  
Reply to Office Action of August 24, 2006

3. Response to the Rejection of Claims 21-23, 27-31, 33, 40-41 under under 35 U.S.C. §112, second paragraph

Claims 21-23, 27-33, and 40-41 stand rejected under 35 USC §112, second paragraph. This rejection is respectfully traversed by the amendment.

Claims 21-23, 27-33, and 40-41 have been canceled. New Claims 51-67 have particularly pointing out and distinctly claimed the subject matter which the Applicants regard as their invention.

Accordingly, Applicants respectfully request withdrawal of the rejection based upon 35 U.S.C. §112, second paragraph.

4. Response to the Rejection of Claims 21-23, 27-33, and 40-41 under under 35 U.S.C. §103(a)

Claims 21-23, 27-33, and 40-41 are rejected under 35 USC §103(a) as being unpatentable over Shaw (U.S. Patent No. 4,904,584) in view of the Capon et al. (U.S. Patent No. 5,116,964). This rejection is respectfully traversed.

Claims 21-23, 27-33, and 40-41 have been canceled. Applicants' response is directed to the new independent Claim 51, in view of the prior art of record.

A determination under 35 U.S.C. §103 is whether the claimed invention as a whole would have been obvious to a person of ordinary skill in the art at the time the invention was made. *In re Mayne*, 104 F.3d 1339, 1341, 41 USPQ 2d 1451, 1453 (Fed. Cir. 1997). An obviousness determination is based on underlying factual inquiries including: (1) the scope and content of the prior art; (2) the level of ordinary skill in the art; (3) the differences between the claimed invention and prior art; and (4) the objective evidence of nonobviousness. *Graham v. John Deere Co.*, 383 U.S. 1, 17-18, 148 USPQ 459, 467 (1966), see also *Robotic Vision Sys., Inc. v. View Eng'g Inc.*, 189 F.3d 1370 1376, 51 USPQ 2d 1948, 1953 (Fed. Cir. 1999).

Application No. 10/609,346  
Response Dated November 21, 2006  
Reply to Office Action of August 24, 2006

Applicant submits that nothing in the art of record teaches or suggests the subject matter positively recited in the Claim 51. As recited in Claim 51, Applicants' claimed comprising a member selected from the group consisting of (a) a polynucleotide encoding a polypeptide as set forth in SEQ ID NO. 8; and (b) a polynucleotide contained in ATCC Deposit No: PTA-4607.

Shaw teaches site-specific homogeneous modification of polypeptides by attachment of compounds having amine reactive groups. Shaw merely teaches G-CSF is suitable for such a modification.

As pointed out by the Examiner, Shaw fails to teach a polynucleotide encoding both G-CSF and albumin to obtain a fusion protein comprising G-CSF and albumin to increase the half-life of G-CSF.

Shaw's deficiencies are not overcome by Capon et al.

Capon et al. teach nucleic acid encoding a polypeptide fusion comprising a ligand binding partner protein fused to a stable plasma protein. The ligand binding partner are proteins known to function to bind specifically to target ligand molecules, and are generally found in their native state as secreted or membrane bound polypeptides. Capon et al. teach that the stable plasma protein extends the in vivo plasma half-life of the ligand binding partner when present as a fusion with the ligand binding partner.

Furthermore, Capon et al. specifically teach that a large number of proteins having various structures, sources, and biological functions are not suitable, therefore, excluded from the ligand binding partner of their invention.

Capon et al. fail to teach Applicants' claimed polynucleotide encoding a polypeptide as set forth in SEQ ID NO. 8, or a polynucleotide contained in ATCC Deposit No: PTA-4607, which encodes albumin and G-CSF to obtain a HSA/G-CSF fusion protein.

The Examiner states that it would have been prima facie obvious to one having ordinary skill in the art to modify the polynucleotide of Shaw such that it includes both the polynucleotide encoding G-CSF and the polynucleotide encoding

Application No. 10/609,346  
Response Dated November 21, 2006  
Reply to Office Action of August 24, 2006

albumin, to obtain a chimeric protein with an increased circulating half-life.

Applicants respectfully disagree.

First, *In re Dow Chem.*, 837 F.2d 469, 473, 5 USPQ 2d 1529, 1531 (Fed. Cir. 1988), the case law has clearly stated that "the consistent criterion for determination of obviousness is whether the prior art would have suggested to one of ordinary skill in the art that this process should be carried out and would have a reasonable likelihood of success, viewed in the light of the prior art." Therefore, the first requirement is that a showing of a suggestion, teaching or motivation to combine the prior art references is an "essential evidentiary component of an obviousness holding." *C.R. Bard, Inc. v. M3 Sys. Inc.*, 157 F.3d 1340, 1352, 48 USPQ 2d 1225, 1232 (Fed. Cir. 1998). This showing must be clear and particular, and broad conclusory statements about the teaching of multiple references, standing alone, are not "evidence." *In re Dembiczak*, 175, F.3d 994, 1000, 50 USPQ 2d 1614, 1617.

The second requirement is that the ultimate determination of obviousness must be based on a reasonable expectation of success. *In re O'Farrell*, 853 F.2d 894, 903-904, 7 USPQ 2d 1673, 1681 (Fed. Cir. 1988); see also *In re Longi*, 759 F.2d 887, 897, 225 USPQ 645, 651-52 (Fed. Cir. 1985). The mere fact that the prior art may be modified in the manner suggested by the Examiner does not make the modification obvious unless the prior art suggested the desirability of the modification. *In re Fritch*, 972 F.2d 1260, 1265, 23 USPQ 2d 1780, 1783-84 (Fed. Cir. 1992).

In the present case, neither Shaw nor Capon et al. suggests or indicates the modification of Shaw's G-CSF to include the polynucleotide encoding G-CSF and the polynucleotide encoding albumin to obtain Applicants' claimed HSA/G-CSF fusion protein that is bioactive and has a substantially longer shelf life and plasma half-life than G-CSF alone.

Applicants respectfully point out it is well known to a molecular biologist that without undue experimentations to actually express a specific fusion protein and testing its property and bio-activity in vitro and in vivo, one can not predict whether a

Application No. 10/609,346  
Response Dated November 21, 2006  
Reply to Office Action of August 24, 2006

fusion protein retains the structure of the original proteins which are responsible for the biological functions and its actual bio-activity.

Therefore, in the absence of a clear and particular showing from either reference and without a reasonable expectation of success, one skilled in the art would not be motivated to combine the two references, in the manner suggested by the Examiner, to obtain Applicants' claimed invention.

Second, as described above, Capon et al. specifically teach that a large number of proteins having various structures, sources, and biological functions are excluded from the ligand binding partner suitable for their invention. Among those, Capon et al. specifically teach colony stimulating factor 1 receptor is excluded.

There are four subclasses of human colony stimulating factor (CSF) proteins which can be defined according to the types of cells found in the resultant colonies. One subclass, CSF-1, results in colonies containing predominantly macrophages. Other subclasses produce colonies which contain both neutrophilic granulocytes and macrophages (GM-CSF); which contain predominantly neutrophilic granulocytes (G-CSF); and which contain neutrophilic and eosinophilic granulocytes, macrophages, and other myeloid cell types (basophils, erythrocytes, and megakaryocytes) (IL-3).

Applicants respectfully point out because Capon et al. specifically teach CSF-1 receptor is not suitable for their invention, as its binding partner, CSF-1 is not taught by Capon et al. G-CSF, also referred to as CSF-3, is one of the four subclasses of human colony stimulating factor (CSF) proteins, closely related to CSF-1. Based on Capon et al.'s specific exclusion, one skilled in the art would understand that Capon et al. does not suggest CSF receptors, and hence their binding partners, CSF proteins.

Based on the above analysis, one skilled in the art would not be motivated to try to combine Shaw and Capon et al., as suggested by the Examiner, to obtain Applicants' claimed invention.

Third, the motivation to modify cannot derive from Applicant's specification. The Federal Circuit has repeatedly warned that the requisite motivation must come

Application No. 10/609,346  
Response Dated November 21, 2006  
Reply to Office Action of August 24, 2006

from the prior art, not applicant's specification. *In re Dow Chem. Co.*, 837 F.2d 49, 473, 5 U.S.P.Q.2d 1529, 1531-32 (Fed. Cir. 1988), the case law has stated "[t]here must be a reason or suggestion in the art for selecting the procedure used, other than the knowledge learned from the applicant's disclosure." *In re Lee*, 277 F.3d at 1343, *W.L. Gore v. Garlock, Inc.*, 721 F.2d 1540, 1553, 220 USPQ 303, 312-13 (Fed. Cir. 1983), the case law states it is improper to "[use] that which the inventor taught against its teacher."

In the present case, the only teaching of Applicants' claimed HSA/G-CSF fusion protein possessing the desired properties described above is originated from Applicants' own specification. It is apparent that the Examiner has, by hindsight, merely based on what is only taught by the Applicants to suggest the motivation to modify the prior art teachings.

Therefore, Applicant maintains that Applicant's claimed invention as defined by the amended Claim 51 is not obvious in view of the art of record.

With regard to Claims 52-67, as described above, these claims are dependent claims of independent Claim 51. Under the principles of 35 U.S.C. §112, 4<sup>th</sup> paragraph, all of the limitations of each independent claim are recited in its respective dependent claims. As described above, independent Claim 51 is unobvious in view of the prior art of record, as such Claims 52-67 are submitted as being allowable over the art of record.

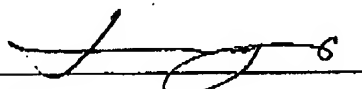
Accordingly, Applicant respectfully requests withdrawal of the rejection based upon 35 U.S.C. §103(a).

It is respectfully submitted that Claims 51-67, the pending claims, are now in condition for allowance and such action is respectfully requested.

Application No. 10/609,346  
Response Dated November 21, 2006  
Reply to Office Action of August 24, 2006

Applicant's Agent respectfully requests direct telephone communication from the Examiner with a view toward any further action deemed necessary to place the application in final condition for allowance.

11/21/2006  
Date of Signature

By:   
Yi Li  
Registration No. 44,211  
Telephone: 305-776-2450

Please address all correspondence to:  
Customer Number 27165